Remarks

The Invention

The claims are directed to a solid, self-bioadhesive composition for topical application to oral mucosal tissue to which it adheres. The composition comprises a bioactive amount of at least one herbal active agent: a bioactive herb, herbal extract, tincture, essential oil, or mixture thereof; or an analgesic, anti-inflammatory, antihistamine, antigen, steroid other than an anti-inflammatory, antimicrobial drug, vitamin, enzyme, antipyretic, antimalarial, antiulcer drug, peptide, or combination thereof. The composition further comprises a pharmaceutically acceptable solid bioadhesive carrier present in an amount from about 40 to about 99 percent by weight of the whole composition. Claims 4, 6, 7, 8, 9, 10, 11, 19, 20, and 25 are specific to herbal formulations.

The compositions can be prepared by forming a solid powder of an herbal active agent by drying the herbal liquid extract with an inert compound. The dried herbal extract powder is mixed with the bioadhesive component and one or more lubricants and the mixture is compressed into tablets of the desired size and shape. These compositions, and in particular those formed into the disks of claims 2 and 3, are prepared by *compression molding* rather than solvent casting. Solvent casting typically requires drying at elevated temperatures in order to remove the solvent. Herbal extracts and essential oils can be extremely sensitive to heat and can degrade at elevated temperatures thereby destroying their therapeutic effectiveness.

The bioadhesive carrier is a material that attaches to mucosal tissue upon hydration. The carrier must be capable of maintaining adhesion in moist or wet environments *in vivo*. The final composition is self-adhesive in that it attaches to the site of interest without the need to reinforce its attachment by way of another adhesive which is applied to a backing. The composition should adhere to mucosal tissue for at least 30 minutes, preferably from about 1 to about 24 hours, more preferably from about 3 to about 10 hours, as defined by claims 2 and 3. Suitable bioadhesive carriers include polysaccharides such as cellulose derivatives such as cellulose acetate, carboxymethylcellulose, and hydroxymethyl cellulose and partially esterified polyacrylic acid polymer such as polyacrylic acid polymers crosslinked with polyalkenyl polyethers, as defined by claims 22, 23, and 26. The compositions can further comprise excipients such as humectants, flavoring agents, sweetening agents, coolants, salivating agents, and numbing agents, as defined by claim 24.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-4, 6-12, 14-26, and 38 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement and as including new matter. The rejection appears to be based on the examiner's argument that the phrase "wherein the agent is present in a homeopathic amount, which is less than a therapeutically effective amount" in claim 1.

Referring to page 4 of the office action, the examiner appears to be stating that she believes there is support for the phrase "a solid, self-bioadhesive composition for topical

application that adheres to oral mucosal tissue comprising a therapeutically effective amount of at least one herbal or homeopathic active agent" or one of the listed compounds.

The claims have therefore been amended to use the language identified by the examiner. The very helpful analysis is appreciated.

The claims have also been amended to clarify that the composition contains ***either*** a herbal agent, homeopathic agent or one of the listed agents.

As discussed in more detail below, the carrier has also been amended to restrict the mucoadhesive polymer to a polymer as listed in claims 22 and 26 and described on pages 12 and 13.

Claims 1 and 6 have been amended as suggested by the examiner. Again, the careful analysis is greatly appreciated.

Excerpts from the on-line Encyclopedia Britannica defining carnallite and carnallite salts are enclosed. This should obvious the rejections of claims 14 and 18 and others referencing carnallite salts.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-4, 6-12, 14-26, and 38 were also rejected under 35 U.S.C. 112, second paragraph as lacking enablement. This rejection is respectfully traversed if applied to the amended claims

It is believed that the examiner has indicated on page 7 that once the alleged new matter was replaced with the language "a solid, self-bioadhesive composition for topical application that

adheres to oral mucosal tissue comprising a therapeutically effective amount of " the listed agents, the lack of enablement rejection would be withdrawn.

In response to the statement that applicants have failed to provide a working example, the examiner's attention is again drawn to page 36 of the application as filed, which fully supports enablement of composition as defined by the amended claim.

Although it is believed to no longer be an issue in view of the foregoing amendments, the state statutory definitions of "homeopathic" have been enclosed with this response to further demonstrate that the meaning of this term was well known and understood by those skilled in the art, and not considered "quackery" as indicated by the examiner. Note that laws governing treatment of patients with homeopathic medicine were enacted in numerous states between 1992 and 1995, long before this application was filed. Therefore, unless the examiner has evidence rather than argument based on an obscure website that can rebut the statutory presumption that such medicines and use in treatment thereof was known, regulated under state law, and accepted generally, the examiner must withdraw this rejection.

Rejections Under 35 U.S.C. § 102

Claims 1, 4, 6-8, and 24 were rejected under 35 U.S.C. 102(b) as disclosed by Green, Green, The Herbal Medicine-Maker's Handbook, A Home Manual, 276-285, The Crossing Press, (2000) ("Green"). Claims 1-4, 6-11, 15-17, 22-24, 26 and 38 were rejected under 35 U.S.C. 102(b or e) as disclosed by U.S. Patent No. 6,303,147 to Gillis or WO 97/24109 by Gilis. Claims 1, 4, 6, 15-17, 22-24, 26 and 38 were rejected under 35 U.S.C. 102(b) as disclosed by

U.S. Patent No. 5,719,197 to Kanios, et al. Claims 1, 4, 7, 22, 23, 24, and 26 were rejected under 35 U.S.C. 102(b) as disclosed by EP 0 839 524 to Ronchi, et al. These rejections are respectfully traversed if applied to the amended claims.

Amendments to the Claims

Claim 1 has been amended to define the mucoadhesive polymer as a specific class of mucoadhesive synthetic carboxylic acid containing polymers describes on pages 12 and 13 of the application, including the preferred embodiment referenced on page 13 and claim 26, present in an amount of between 40 and 99 wt%. The term "polyhydric polymers" (which simply means a polymer having at least two hydroxyl groups) has been deleted from claim 22, and the claim has clarified to refer to copolymers of the named polymers.

The Legal Standard

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims. *Hybritech Inc. v Monoclonal Antibodies Inc.*, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 US 947 (1987); *Scripps Clinic & Research Found v. Genentech Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991). The Federal Circuit held in Scripps, 18 USPQ2d at 1010:

> Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . *There must be no difference* between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. (Emphasis added)

A reference that fails to disclose even one limitation will not be found to anticipate, even if the missing limitation could be discoverable through further experimentation. As the Federal Circuit held in Scripps, Id.:

> [A] finding of anticipation requires that all aspects of the claimed invention were already described in a single reference: a finding that is not supportable if it is necessary to prove facts beyond those disclosed in the reference in order to meet the claim limitations. The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill in the gaps in the reference.

For a prior art reference to anticipate a claim, it must enable a person skilled in the art to practice the invention. The Federal Circuit held that "a §102(b) reference must sufficiently describe the claimed invention to have placed the public in possession of it. . . [E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." Paperless Accounting Inc v Bay Area Rapid Transit Sys., 231 USPQ 649, 653 (Fed. Cir. 1986).

Green

Green fails to disclose a bioadhesive polymer as defined by the amended claims, incorporating the polymers of claims 22 and 26, neither of which was rejected over Green.

Green describes the preparation of poultices, which are defined as local baths that utilize warmth and moisture to relax tissue and relieve pain (page 277, second column, 1st paragraph).

Herbal preparations can be incorporated to enhance the therapeutic properties of poultices (page 277, second column, 1st paragraph). Green describes the procedure for making a bentonite clay poultice for the mouth, teeth and gums for reducing the inflammation of an abscessed tooth (page 285). Step 5 instructs the reader to hold the poultice in place. There is no disclosure of using mucoadhesive synthetic polycarboxylic acid polymers. Therefore, Green does not disclose a self-bioadhesive composition as claimed by the applicants.

Gilis

Gilis also does not describe the claimed bioadhesive compositions defined as including mucoadhesive synthetic polycarboxylic acid polymers, as described on pages 12 and 13 of the application. Gilis describes a tablet made from greater than 80% starch (see col. 1, lines 61-65 and col. 2, lines 30-38). This material is not mucoadhesive under the conditions in the oral cavity, nor is it a polycarboxylic acid polymer since it is a polymer of glucose molecules which has free hydroxyl groups but not carboxylic groups. There is a reference to inclusion of hydrophilic polymers but the amount must be less than 10% (col. 1, lines 65-67).

Kanios

Kanios also fails to disclose the claimed mucoadhesive synthetic polycarboxylic acid polymer composition. Kanios uses a natural gum as a polymer (col. 10, lines 32-44), in combination with a clay, solvent and plasticizer (col. 2, lines 22-34), formed using a process involving elevated temperatures, which is highly detrimental to herbal formulations.

Ranchi

Ranchi relates to oral lozenges containing highly water soluble sugars, not the claimed synthetic polymers. Sugars are not polycarboxylic acid polymers but contain hydroxyl groups. See col. 2, lines 1-6. Other excipients can be included in an amount of 0.1 to 50% out of a total excipient concentration of 30 to 99.9% (col. 2, lines 11-23). Out of the long list of possible excipients provided at col. 3, including many non-carboxylic acid polymers and many non-synthetic polymers, in combination with the requirement for a sugar, there is a possibility that the product could include 40 wt % of a polycarboxylic acid polymer. However, it is well established that the mere possibility of a disclosure is not an anticipation; the disclosure must be clear and enabling to one of skill in the art. The active ingredients that can be incorporated are listed at col. 3, lines 32-38 as antibiotics and topical anesthetics. In order to facilitate prosecution, even though it is not believed to be necessary, antibiotics other than herbal and homeopathic agents which may have incidental antibiotic activity have been deleted from the claimed subject matter, thereby clearly mooting the possibility that Ranchi discloses the claimed subject matter.

Rejections Under 35 U.S.C. § 103

Claims 1-4, 6-11, 15-17, 19, 22-24, 26 and 38 were rejected under 35 U.S.C. 103 as obvious over Gilis in combination with U.S. Patent No. 5,939,050 to Iyer, et al. and U.S. Patent No. 6,197,305 to Friedman, et al., along with Lawless, The Illustrated Encyclopedia of Essential Oils, Element Books, 1995 ("Lawless"). Claims 1-4, 6-12, 15-17, 19, 22-24, 26 and 38 were rejected under 35 U.S.C. 103 as obvious over Gilis in combination with Friedman and U.S.

Patent No. 6,207,137 to Shuch. These rejections are respectfully traversed if applied to the amended claims.

The Legal Standard

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

"There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998) (The combination of the references taught every element of the claimed invention, however without a motivation to combine, a rejection based on a prima facie case of obvious was held improper.). The level of skill in the art cannot be relied upon to provide the suggestion to combine references. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). "In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be

sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Gilis

Gilis is discussed above.

Iyer

U.S. Patent No. 5,939,050 to Iyer *et al.* ("Iyer") describes antimicrobial compositions comprising at least two antimicrobial agents which exhibit reduced MIC values relative to the MIC values for the agents making up the combination when measured alone (abstract). Suitable plant extracts and essential oils which can be used as antimicrobial agents are described at col. 5, line 49 to col. 6, line 27). Iyer does not disclose a solid, self-bioadhesive tablet formulation for topical application that adheres to the oral mucosal tissue. As noted at col. 7, lines 16-27 and lines 53-61, these formulations are oral rinses, mouth wases or cleansers.

Friedman

U.S. Patent No. 6,197,305 to Friedman *et al.* ("Friedman") discloses an anti-fungal composition containing (a) an extract of botanical materials; and (b) an essential oil, in a defined amount that is therapeutically effective (col. 2, lines 20-59; col. 4, lines 5-9; see also examples at col 6-10). Friedman discloses that the compositions are suitable for local oral, mucosal, topical, intra-nasal, and intra-vaginal administration. Friedman does not disclose a solid, self-bioadhesive composition for topical application that adheres to the oral mucosal tissue. The

formulations are not bioadhesive. Ingredients such as those at col. 7 are either hydrophobic (such as beeswax) or liquid (glycerin and oil) or contain detergent (such as sodium lauryl sulfate). Table 3 is liquid, not solid. Table 4 is a gel primarily of polyethylene glycol, which is not bioadhesive alone. Table 7 is similar. Tables 5 and 6 are hydrophobic skin cream. Example 10 contains similar examples to the other examples.

Lawless

Lawless discloses that the essential oil of lemon contains approximately 70% limonene as well as sabinene, myrcene, and pinenes (page 120). Lawless does not disclose a self-bioadhesive composition for topical application that adheres to oral mucosal tissue.

Shuch

Shuch discloses an orally absorbable dental formulation which includes a base to which one or more active components, such as vitamin C and co-enzyme Q-10, can be added (abstract). The composition can be a toothpaste, mouthwash, or chewing gum (col. 2, lines 5-9) and can be used in conjunction with dental treatments such as prophylaxis paste and irrigation fluids (col. 2, lines 9-13). Formulations such as toothpastes, mouthwashes and chewing gums have short contact times, typically on the order of a few seconds.

As described in the specification, the claimed bioadhesive tablet formulations adhere to the oral mucosal tissue for at least 30 minutes, preferably from about 1 hour to 24 hours, more preferably from about 3 hours to about 10 hours. Shuch does not disclose or even suggest a solid self-bioadhesive composition for topical application that adheres to oral mucosal tissue, nor

a pharmaceutically acceptable solid bioadhesive carrier in an amount from about 40 to 99 percent based on the weight of the whole composition in a form suitable for administration and adhesion to the oral mucosa.

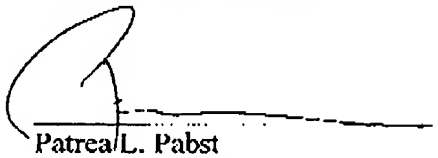
Summary

In summary, the prior art fails to disclose each claimed element and the motivation to modify what is disclosed and combine it as applicants have done. There is no recognition in the prior art of the use of 40-99 2t % polycarboxylic acid to make a tablet which is mucoadhesive and adheres to the oral cavity and which is prepared using a method that allows incorporation of labile materials such as herbs. It is well established that it is not sufficient to merely identify art and then assert that it would be obvious to combine: the motivation must come from the references. Such hindsight is impermissible. The prior art must lead one skilled in the art to what is claimed. The art cited by the examiner does not do this.

Nowhere does the prior art provide the motivation to combine these elements as applicants have done. It is well established that it is not sufficient to merely identify art and then assert that it would be obvious to combine: the motivation must come from the references.

For the foregoing reasons, Applicants submit that claims 1-4, 6-12, 14-26, and 38 are patentable.

Respectfully submitted,



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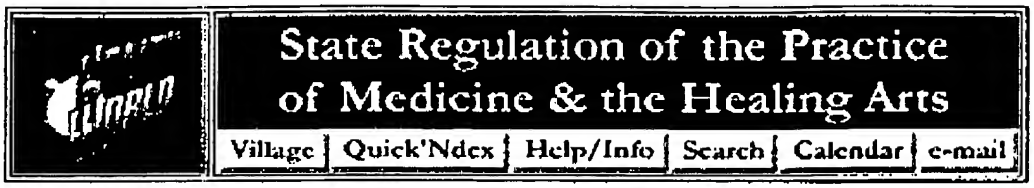

Definition Of Homeopathic

ARIZONA

The statute states: " 'Homeopathy' means a system of medicine employing substances of animal, vegetable or mineral origin which are given in microdosage and prepared according to homeopathic pharmacology, in accordance with the principle that a substance which produces symptoms in a healthy person can cure those symptoms in an ill person. The practice of homeopathy includes acupuncture, neuromuscular integration, orthomolecular therapy, nutrition, chelation therapy, pharmaceutical medicine and minor surgery."

ARIZ. REV. STAT. ANN. § 32-2901(4) (1992).

NEVADA